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Preconception Maternal and Paternal Exposure to Persistent Organic Pollutants and Birth Size: The LIFE Study

Candace A. Robledo,¹ Edwina Yeung,¹ Pauline Mendola,¹ Rajeshwari Sundaram,¹ Jose Maisog,¹ Anne M. Sweeney,² Dana Boyd Barr,³ and Germaine M. Buck Louis¹

¹Division of Intramural Population Health Research, *Eunice Kennedy Shriver* National Institute of Child Health and Human Development, National Institutes of Health, Rockville, Maryland, USA; ²Department of Epidemiology and Biostatistics, School of Rural Public Health, Texas A&M Health Sciences Center, College Station, Texas, USA; ³Emory University, Rollins School of Public Health, Atlanta, Georgia, USA

Address correspondence to Candace A. Robledo, Division of Intramural Population Health Research, *Eunice Kennedy Shriver* National Institute of Child Health and Human Development, 6100 Executive Blvd, Room 7B03S, Rockville, MD 20892-7510 Telephone: (301) 594-9150. Fax: (301) 402-2084. E-mail: robledoc@mail.nih.gov

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Abstract

Background: Persistent organic pollutants (POPs) are developmental toxicants but the impact of both maternal and paternal exposures on offspring birth size is largely unexplored.

Objective: To examine associations between maternal and paternal serum concentrations of 63 POPs, comprising five major classes of pollutants, with birth size measures.

Methods: Parental serum concentrations of 9 organochlorine pesticides, 1 polybrominated biphenyl (PBB), 7 perfluoroalkyl chemicals (PFCs), 10 polybrominated diphenyl ethers (PBDEs) and 36 polychlorinated biphenyls (PCBs) were measured prior to conception for 234 couples. Differences in birth weight, length, head circumference, and ponderal index were estimated using multiple linear regression per 1-standard deviation (SD) increase in natural log-transformed (ln-transformed) chemicals. Models were estimated separately for each parent and adjusted for maternal age, maternal pre-pregnancy BMI (kg/m^2) and other confounders, and all models included an interaction term between infant gender and each chemical.

Results: Among girls ($n = 117$) birth weight was significantly lower (range: 84-195 grams) in association with 1-SD increase in ln-transformed maternal serum concentrations of DDT, PBDE congeners 28 and 183 and paternal serum concentrations of PBDE-183 and PCB-167. Among boys ($n = 113$), maternal (PCBs: 138, 153, 167, 170, 195, and 209, PFOSA) and paternal (PCBs: 172 and 195) serum concentrations of several POPs were statistically associated with lower birth weight (range: 98-170 grams), while paternal concentrations of PBDEs (66, 99) were associated with higher birth weight. Differences in offspring head circumference, length, and ponderal index were also associated with parental exposures.

Conclusions: Preconceptional maternal and paternal concentrations of several POPs were associated with statistically significant differences in birth size among offspring.

Introduction

The presence of persistent organic pollutants (POPs) in maternal blood (Llop et al. 2010; Rodriguez-Dozal et al. 2012; Rudge et al. 2012; Wang et al. 2009), umbilical cord blood (Arbuckle et al. 2013; Foster et al. 2011) and in breast milk (Mikes et al. 2012; Pan et al. 2009; Tanabe and Kunisue 2007) documenting *in utero* and lactational exposure has prompted epidemiological studies to examine the relationship between exposure to these compounds and fetal growth and development (Mattison 2010; Windham and Fenster 2008). Research in this area has generally focused on outcomes such as birth weight and length of gestation, strong indicators of neonatal health. Epidemiological studies have shown a decrease in birth weight in relation to exposure to POPs that include polychlorinated bi-phenyls (PCBs) (Govarts et al. 2012; Karmaus and Zhu 2004; Murphy et al. 2010), polychlorinated diphenyl ethers (PBDEs) (Harley et al. 2011), perfluoralkyl chemicals (PFCs) (Washino et al. 2009) and organochlorine pesticides (Wolff et al. 2007). While the previous studies have demonstrated an association between POPs and lower birth size, proxied by birth weight, findings are inconsistent and studies have also reported null associations (Farhang et al. 2005; Givens et al. 2007; Karmaus and Zhu 2004; Kezios et al. 2012; Longnecker et al. 2005; Mazdai et al. 2003; Olsen et al. 2009; Pan et al. 2009; Sweeney and Symanski 2007; Tan et al. 2009; Wu et al. 2010).

Inconsistencies may be attributed to several key limitations of prior studies. Past research has focused on pre-and post-natal exposures to POPs, despite evidence that the preconception period may be a critical window of exposure for fetal growth and development (Chapin et al. 2004). Given the metabolic and physiological changes that occur during pregnancy, preconception levels may be more accurate in capturing the dose to the fetus. Regardless of their long half-lives and persistent nature, the concentrations of pollutants may vary across critical windows of

development, as seen with PCBs (Bloom et al. 2007) and other selected POPs (Wang et al. 2009). Finally, prior studies have focused on elucidating the impact of maternal exposure to POPs on birth size, irrespective of the fact that pregnancy is a couple-dependent outcome. Consequently, the impacts of paternally mediated factors on birth size have been largely unstudied (Cordier 2008; Shah 2010). Limited to occupational studies, little is known regarding the impact of paternal POP exposures on birth size (Lawson et al. 2004; Michalek et al. 1998).

We aim to address these gaps in knowledge by estimating the associations of maternal and paternal preconceptional serum concentrations of POPs on birth size. We hypothesize that preconceptional serum concentrations of both maternal and paternal persistent environmental chemicals are associated with reduced birth size measures (i.e. birth weight, head circumference, length and ponderal index).

Methods

Study population

The Longitudinal Investigation of Fertility and the Environment (LIFE) Study was a prospective cohort study conducted between 2005 and 2009 to assess the impact of persistent environmental chemicals on reproductive outcomes (Buck Louis et al. 2011). Briefly, LIFE recruited couples (n = 501) that resided in Michigan and Texas with reported or presumed exposure to persistent environmental chemicals. Married couples or those in a committed relationship who were planning a pregnancy in the next 6 months were targeted for recruitment. Couples were ineligible to participate if either partner was medically/surgically sterile; they had discontinued contraception for more than 2 months; female's menstrual cycle was not between 21-42 days or she had received injectable contraceptives within the previous 12 months; they were not of

reproductive age (females < 18 or > 40 years and males: \leq 18 years) or they could not communicate in English or Spanish. Couples were followed until a positive human chorionic gonadotropin (hCG) pregnancy or through 12 months of attempting pregnancy. Following conception, women were followed daily for 8 weeks and then monthly until a pregnancy loss or delivery. Analyses were restricted to couples for which a singleton delivery was observed (n = 247), irrespective of a previous loss, and for which birth weight was reported (n = 234). In doing so, we excluded data for two sets of twin births. Institutional review board approval was obtained from all collaborating institutions and informed written consent was obtained from all couples prior to their participation.

Assessment of fetal growth outcomes and covariates

Couples were asked to report birth size characteristics for the index birth using standardized birth announcements specifically designed for the LIFE study that were included in the pregnancy diary (available upon request). Women were trained in their use and completeness after delivery. Information recorded on the delivery cards included infant gender, birthweight (in grams or pounds and ounces) (n = 230), length (in centimeters or inches) (n = 229) and head circumference (in centimeters or inches) (n = 181). Ponderal index (n = 229), a marker of asymmetrical growth retardation thought to be a result of fetal insult, was defined as $100 \times [\text{birth weight (g)/length (cm}^3\text{)}]$ (Sparks JW et al. 1998). Analyses did not include infants whose birth weight (n = 2) or head circumference (n = 2) exceeded the 99th percentile.

Baseline questionnaires were administered to each partner separately and were used to collect medical and reproductive histories. Information on lifestyle factors such as the use of alcohol and tobacco in the previous 12 months was also collected. Participants then underwent an

anthropometric assessment (Lohman TG et al. 1988) for measurement of their height and weight. Body mass index (BMI) was calculated as weight (kg)/height (m²).

Daily journals captured data on lifestyle factors, sexual intercourse and home pregnancy test results. A fertility monitor captured data on peak luteinizing hormone concentrations indicative of ovulation. These data combined with information on sexual intercourse and positive hCG pregnancy test results allowed for the estimation of day of conception and, thereafter, a postconception gestational age. Pregnant women were asked to complete daily pregnancy journals that captured information on weight gain and gravid diseases (e.g. gestational diabetes).

Exposure assessment

Biospecimens were collected from each partner during the baseline home visit. Approximately 20 mL of nonfasting blood were collected to measure concentrations of environmental chemicals. For quality control, blood collection equipment was tested and determined to be free from contaminants under study. Quantification of serum toxicants was conducted by the Division of Laboratory Sciences in the National Center for Environmental Health at the Centers for Disease Control and Prevention. A list of all congeners measured and their abbreviations can be found in Table 1. Established protocols using isotope dilution gas chromatography-high resolution mass spectrometry or high performance liquid chromatography-tandem mass spectrometry (Barr et al. 2003; Kuklennyik et al. 2005; Sandau et al. 2003) were used to estimate serum concentrations of one polybrominated biphenyl (PBB), nine organochlorine pesticides (OCPs), ten polybrominated diphenylethers (PBDEs), thirty-six polychlorinated biphenyls (PCBs) and seven perfluoralkyl chemicals (PFCs). Liquid chromatography-isotope dilution tandem mass spectrometry (Bernert, Jr. et al. 1997) was used to quantify serum concentrations of

cotinine (ng/ml), as a measure of tobacco exposure. Enzymatic methods were used to estimate total cholesterol, non-esterified cholesterol, triglycerides and phospholipids (Akins et al. 1989). Total serum lipids (ng/g serum) were calculated using established summation methods (Bernert et al. 2007; Phillips et al. 1989). Serum lipid concentrations were included in models as a covariate, and pollutant concentrations are reported in ng/g serum; except for PFCs and cotinine that are reported in ng/mL.

Statistical analyses

We assessed the distributions of all exposures and relevant covariates. Normality of continuous variables was assessed using Kolmogorov-Smirnov tests. Missing covariate values and missing chemical, cotinine and lipid data (< 4%), due to insufficient blood for analysis, were imputed under the missing at random assumption, using Markov Chain Monte Carlo methods (Rubin 1996) detailed elsewhere (Buck Louis et al. 2013). Machine-read values for chemical concentrations were used and values below the limit of detection were not substituted to avoid introducing bias (Schisterman et al. 2006). To account for skewed distribution and for ease of interpretation, chemical concentrations were natural log-transformed (ln) and rescaled by their standard deviation. Geometric means (GM) and 95% confidence intervals were calculated for all chemicals. See Supplemental Material, Table S1, for a list of standard deviations and geometric means for this study population. The outcome variables, birth weight (grams), head circumference (cm), length (cm) and ponderal index (g/cm^3) were not ln-transformed. Each outcome and chemical concentration was modeled as a continuous variable.

Multiple linear regression was used to estimate the mean difference in each outcome per 1-standard deviation (SD) increase for all ln-transformed chemicals. The mean differences in

growth outcomes for each chemical and parent were estimated separately. Models were adjusted *a priori* for maternal age, the difference between maternal and paternal age, maternal pre-pregnancy BMI (kg/m^2), infant gender, serum lipids (except PFCs) and serum cotinine concentrations (Cliver et al. 1995; Cogswell and Yip 1995; Shah 2010). The sum of the remaining chemical concentrations (ln-transformed and scaled by their respective standard deviation) in each chemical's respective class was included in models to account for the mean level of individual concentrations. To account for their partner's exposure, each model also included the total sum of partner's serum concentrations in the respective class for the chemical being evaluated. Interaction between each pollutant and infant gender was evaluated by examining the statistical significance of their product term in each model ($p < 0.05$). Evidence of interaction between chemical exposures and birth outcomes by infant gender was observed for some chemicals and models by significant interaction term ($p\text{-interaction} < 0.05$) and thus all associations were estimated stratified by gender for consistency. We report associations for chemicals for which at least one statistically significant association was estimated with birth size measures. Statistical significance was set at $p < 0.05$.

A sensitivity analysis was conducted that excluded pregnancies complicated by gestational diabetes or hypertension because of their known effects on fetal growth (Mayer and Joseph 2013). Results and conclusions of the association between parental preconception exposure to persistent organic pollutants and birth size measures did not vary (data not shown). Therefore, model estimates that include all pregnancies are reported.

Results

Study population

Partners for whom a singleton delivery occurred were very similar in their socio-demographic characteristics (Table 2). The majority of men and women were Non-Hispanic White, had a college education, were insured, and did not smoke or drink alcohol. Compared with their female counterparts, males were approximately 2 years older and on average had a higher BMI (29.3 versus 26.5 kg/m²). Women reported having gestational diabetes mellitus (n=27), hypercholesterolemia (n=18) and pre-existing hypertension (n = 7). The majority of infants were female (51%). The mean postconception gestational age and birth weight of infants at delivery was 36.2 weeks (SD = 2.2) and 3382.3 grams (SD = 487.5), respectively.

Serum concentrations of most POPs among couples were similar for partners. However, geometric mean concentrations of pesticides such as *p,p'*-DDE (0.580 ng/g ; 95% CI: 0.534, 0.630 versus 0.752 ng/g ; 95% CI: 0.700, 0.808), mirex (0.007 ng/g ; 95% CI: 0.007, 0.008 versus 0.013 ng/g; 95% CI: 0.011, 0.014) and several PFCs were markedly higher among males (see Supplemental Material, Table S1). Preconceptional parental concentrations of POPs were found to be associated with changes in birth size measures.

Organochlorine pesticides and PBB

Statistically significant differences in birth size measures were estimated in association with both maternal and paternal preconception serum concentrations of organochlorine pesticides among girls, but virtually no significant associations were observed among boys (Table 3). Please see Supplemental Material, Tables S2-S5, for all estimated associations for birth size measures and chemicals evaluated in our study. Among girls, a 1-SD increase in ln-transformed maternal

serum concentrations of *o,p'*-DDT was associated with lower birth weight ($\beta = 195.39$ grams; 95% CI: -351.25, -39.52), driven perhaps by smaller head circumference ($\beta = -0.78$ cm; 95% CI: -1.48, -0.09). Smaller head circumference was also seen with increasing maternal concentrations of β -HCH ($\beta = 1.47$ cm; 95% CI: -2.33, -0.61). Length among girls was inversely associated with maternal concentrations of γ -HCH (lindane) and subsequently higher ponderal index ($\beta = 0.09$ g/cm³, 95% CI: 0.03, 0.16). Similarly, paternal concentrations of γ -HCH were associated with shorter length and higher ponderal index among girls despite mutual adjustment for mean partner concentrations of other organochlorine exposure. A higher ponderal index among girls was also seen with increasing paternal concentrations of *p,p'*-DDE. Except for larger head circumference observed with increasing maternal concentrations of HCB, preconceptional parental concentrations of organochlorine pesticides were not associated with birth size among boys. Parental preconceptional concentrations of PBB 153 were not found to be associated with birth size measures.

PFCs

The mean birth weight of boys was 104.23 grams lower (95% CI: -194.16, 14.30) for every 1-SD increase in ln-transformed maternal concentrations of PFOSA. Maternal concentrations of the Et-PFOSA-AcOH metabolite were associated with a smaller mean ponderal index among girls (-0.09 g/cm³; 95% CI: -0.16, -0.02). We did not observe associations between and preconceptional paternal concentrations of PFCs and birth measures. Furthermore, preconceptional parental concentrations of PFCs were not associated with length or head circumference at birth.

PBDEs

Maternal concentrations of PBDEs were associated with significant differences in mean birth weight in boys and girls. Maternal concentrations of PBDE congeners 28 and 183 were associated with lower birth weight among girls; the largest negative association was estimated for PBDE 28 ($\beta = -151.33$ grams; 95% CI: -298.56, -4.10). Maternal concentrations of PBDE 28 were also statistically associated with smaller length and head circumference among girls. On the contrary, for every 1-SD increase in ln-transformed maternal concentrations of PBDE 66 and 99, mean birth weight among boys was 125.04 grams (95% CI: 18.16, 231.92) and 133.39 grams (95% CI: 9.12, 257.37) higher, respectively. Among boys, PBDE congeners were also statistically associated with larger length (PBDE 99) and head circumference (PBDE 66, 85, 99). As seen with maternal concentrations, paternal concentrations of PBDE 183 were also significantly associated with lower birth weight among girls ($\beta = -92.13$ grams, 95% CI: -173.44, -10.82).

PCBs

Among girls, maternal concentrations of PCBs were not associated with significant differences in birth weight. However, for every 1-SD increase in ln-transformed concentrations of paternal concentrations of PCB 167, the mean birth weight among girls was 97.49 grams lower (95% CI: -187.45, -7.54), mean length ($\beta = -0.57$ cm, 95% CI: -1.12, -0.02) and head circumference ($\beta = -0.45$ cm, 95% CI -0.86, -0.03) were smaller. Significant associations between parental concentrations of PCBs and birth size were more frequent among boys. Birth weight among boys was lower by between 99-170 grams per 1-SD increases in ln-transformed maternal (PCB 138, 153, 167, 170, 195 and 209) and paternal (PCB-172, 195) concentrations. Maternal

concentrations of PCBs were statistically associated with smaller head circumference in girls (PCB 138) and boys (PCB128, 138, 153). Paternal concentrations of PCBs were also significantly associated with smaller head circumference among girls (PCB 167) and boys (PCB 128, 157). Maternal concentrations of PCB 201 and 206 were associated with larger head circumference. Maternal concentrations of PCB 138 were associated with lower mean birth weight among boys and smaller mean head circumference and ponderal index among boys and girls. Paternal concentrations of PCB 138 were only estimated to be associated with smaller mean ponderal index among boys. Additionally, in girls, paternal concentrations of PCB 156 and in boys maternal (PCB 170, 172) and paternal (PCB 156, 157) PCB concentrations were associated with smaller ponderal index (range: 0.08 – 0.13 g/cm³).

Persistent organic pollutants associated with multiple birth size outcomes

Both maternal and paternal concentrations of several persistent organic pollutants were associated with statistical differences in the same birth size measure among their offspring. The statistical differences associated with increasing parental concentrations of these pollutants were often of similar magnitude and direction. We briefly highlight these compounds here.

Lower mean birth weight was observed in association with increasing preconception maternal and paternal concentrations of PBDE 183 among girls and PCB 128 and 195 among boys. Maternal concentrations of PCB 167 were associated with lower mean birthweight among girls only, but paternal concentrations were associated with lower birth weight in boys. Increasing maternal and paternal concentrations of γ -HCH were associated with smaller head circumference and higher ponderal index among girls.

Discussion

In this prospective pregnancy study with preconception enrollment of couples, we demonstrated that both preconception maternal and paternal serum concentrations of persistent organic pollutants were significantly associated with birth size measures among their offspring even after taking into account their partner's serum concentrations. In addition, we also report several statistically significant differences in birth size measures by infant gender and between and within classes of pollutants. We observed decreases in infant birth weight between 85-195 grams with 1-SD increases in preconception maternal and paternal serum concentrations of POPs.

This reduction is similar in magnitude to what has been reported for other prenatal maternal environmental exposures. Compared to nonsmokers, lower mean birth weight has been reported for infants born to women who reported cigarette smoking during the first trimester or throughout pregnancy (range: 55-189 grams) (Cliver et al. 1995). Meta-analyses have reported lower birth weight among infants born to non-smoking women exposed to environmental tobacco smoke (33 grams, 95% CI: 16, 51) (Leonardi-Bee et al. 2011) and in association with increasing cord serum concentrations of PCB 153 (150 grams, 95% CI: 50, 250) (Govarts et al. 2012). Lastly, a meta-analysis reported when compared to lower exposure groups, women exposed to higher mean levels of indoor air pollution from solid fuel use had infants whose birth weight was approximately 96.6 grams lower (95% CI: 68.5, 124.7) (Pope et al. 2010).

Our findings underscore the importance of designing epidemiological studies that ascertain preconception parental exposures in relation to birth size measures. In addition, given that paternal environmental exposures are often overlooked when examining the associations between parental exposures and fetal growth, there is a need for more comprehensive

investigations of the associations between preconception paternal exposures and fetal growth and development. Both maternal and paternal serum concentrations of several pollutants (PBDE 183, PCBs 128, 138, 167, 195 and γ -HCH) were associated with birth size measures but more research is needed to investigate whether associations that were specific to paternal serum concentrations are relevant and can be confirmed in other populations.

There are few prospective pregnancy studies that report parental preconception serum concentrations of POPs, making it difficult to further evaluate our findings. The only known study to examine the association between preconception maternal PCB levels and birth weight was conducted using data obtained from a prospective cohort of New York Anglers and their partners planning a pregnancy within the next 6 months. After adjustment for maternal height, smoking and infant sex, the birth weight of infants ($n = 50$) born to mothers with the highest concentrations of antiestrogenic PCBs (IQR: 0.23-0.33 ng/g serum) was approximately 471 grams (95% CI: -890.2 to -51.3) lighter than infants born to mothers with the lowest concentrations (IQR: 0.13-0.15 ng/g serum). This study also examined the association between infant birth weight and maternal antiestrogenic PCB concentrations from serum measured during the prenatal period (median: 6 weeks gestation). The mean difference in infant birth weight between women with the highest (IQR: 0.15-0.21 ng/g serum) and lowest (IQR: 0.07-0.09 ng/g serum) prenatal concentrations of maternal antiestrogenic PCBs was approximately 210 grams less ($\beta = -260.5$, 95%CI: -667.4, 146.5) than what was reported for preconception levels (Murphy et al. 2010).

Given the debate about classifying chemicals by their action, which may also be a function of dose, we decided to examine each individually. By doing so, we do not make any assumptions

regarding their hypothesized biologic activity or how compounds may interact with each other in mixture form. However, in our present study we report statistically significant associations between birth size measures and two PCB congeners; for one previously shown to be estrogenic (PCB 153) we found maternal concentrations were significantly associated with lower birthweight and head circumference in boys and for another, shown to be antiestrogenic (PCB 156), we found paternal concentrations to be associated with lower ponderal index in both boys and girls (Cook et al. 2001). We also observed associations between birth weight and lower serum concentrations of PCBs than what has been previously published study of New York Anglers and their partners planning a pregnancy mentioned previously (Murphy et al. 2010). It has been shown that serum concentrations of POPs in the LIFE study population (Buck Louis et al. 2013) are lower than reported for the US population (Centers for Disease Control and Prevention 2013). This difference is not surprising given that concentrations of persistent chemicals increase with age and the LIFE cohort is comprised of couples of reproductive age, unlike the NHANES population that comprised of women aged 12 to 85 years of age.

Our study also reports several positive associations between pollutants and birth size measures. Maternal concentrations of PBDE 66 and 99 were associated with increased mean birth weight, length, and head circumference among boys only. Maternal concentrations of PCBs (201, 206) and maternal and paternal concentrations of organochlorine pesticides were associated with increased mean head circumference and ponderal index among girls only. While not comparable to our study, other studies have reported positive associations between maternal prenatal levels of environmental chemicals. Maternal prenatal concentrations of total PCBs and PBBs (congener specific information not available) have been associated with higher birth weight (Sweeney and Symanski 2007). Positive associations between head circumference and length have also been

reported for maternal prenatal levels of organophosphate pesticides not evaluated in this study (Eskenazi et al. 2004). Associations reported by these studies also differed by gender. We are unable to explain these findings but posit that they may reflect differing structural activity or biological activity of individual congeners; particularly given that associations differed by infant gender. Also, the windows of vulnerability for a fetus' growth and development may differ by congener. We also speculate these positive associations may be confounded by healthy behaviors such as the consumption of fish or anti-oxidant rich foods. These healthy behaviors, although potential sources of parental POP exposure, may also positively impact fetal growth and development.

Our study addressed several key limitations of prior studies with equivocal findings of the association between prenatal exposure to POPs and birth size. For one, many studies ascertained prenatal exposure to POPs during late pregnancy using maternal serum concentrations at the time of delivery or using umbilical cord serum concentrations. These studies may not be capturing exposure during relevant windows of fetal growth and development. Prospective pregnancy cohort studies that recruit couples discontinuing contraception to become pregnant are rare and this is the only way to examine the association between preconceptional exposures to persistent organic pollutants with human birth size. Despite their long half-lives, it has been shown that maternal serum concentrations of PCBs and selected POPs can vary across critical windows of human reproduction and development during pregnancy (Bloom et al. 2007; Wang et al. 2009). Preconceptional maternal serum concentrations are not influenced by the expansion of blood volume and changes in metabolism associated with normal pregnancy. As such, we can explore associations with birth size measures in relation to exposure that reflects preconception and early pregnancy, a key window for these effects.

Prior studies have focused on maternal exposures and how they impact developmental health. Paternal exposures to POPs have been largely unstudied and little is known about their potential impact on fetal development and growth. Environmental chemical exposures that occur during spermatogenesis may impact the quality of a father's gametes and, therefore, may affect the susceptibility and health of his offspring *in utero* or after birth (Olshan and Faustman 1993). Epigenetic changes in gametes caused by transient paternal exposures may be stably transferred to multiple generations (Anderson 2005; Fullston et al. 2013). Many studies have reported global epigenetic changes in different cell types in association with environmental chemical exposures (Curley et al. 2011). In regards to past research, the burden faced by participants in collecting biological specimens, as well as the cost of analyzing samples has limited studies. Therefore, studies of the association between environmental toxicants and birth size focus on select chemicals or a specific class of compounds. In our study we were not limited to studying a particular class or select group of analytes. We were able to examine the association between birth measures of interest and 63 chemicals, comprising 5 major classes of POPs (organochlorine pesticides, PBB, PBDEs, PCBs and PFCs).

Due to sample size limitations we were unable to examine the associations between parental preconception levels of POPs and growth restriction or low birth weight. However, we were still able to estimate statistically significant associations in this preconception cohort. Another limitation is the reliance on maternal reported birth measures which may be biased. Although maternal recall of birth weight has been shown to be accurate and reliable (Adegboye and Heitmann 2008; Bat-Erdene et al. 2013; Buka et al. 2004), the normal flexed condition and head molding of the neonate at delivery may lead to measurement error of length (Shinwell and Shlomo 2003) and head circumference, respectively. However, measurement/reporting errors

should not be correlated to chemical concentrations and our estimates may have been biased toward null. We also did not control for multiple comparisons, given the exploratory nature of this work and our intent to identify signals for the preconception window that would require follow-up research. For each outcome, 189 comparisons were undertaken. We would have expected to observe 10 significant findings by chance alone when assessing maternal and paternal exposures. We observed 16 for birth weight, 5 for length, 16 for head circumference and 12 for ponderal index. We observed more than the expected number of significant results by chance alone, though we still urge caution in the interpretation of our findings.

To our knowledge, this study is the first to investigate preconceptional and paternal measures of environmental chemicals in association with birth size. Our findings suggest that many of these chemicals are associated with reduced birth size measures even at low levels of exposure, and support the need for continued rigor in reducing and perhaps eliminating exposures.

References

- Adegboye AR, Heitmann B. 2008. Accuracy and correlates of maternal recall of birthweight and gestational age. *BJOG* 115:886-893.
- Akins JR, Waldrep K, Bernert JT, Jr. 1989. The estimation of total serum lipids by a completely enzymatic 'summation' method. *Clin Chim Acta* 184:219-226.
- Anderson D. 2005. Male-mediated developmental toxicity. *Toxicol Appl Pharmacol* 207:506-513.
- Arbuckle TE, Kubwabo C, Walker M, Davis K, Lalonde K, Kosarac I, et al. 2013. Umbilical cord blood levels of perfluoroalkyl acids and polybrominated flame retardants. *Int J Hyg Environ Health* 216:184-194.
- Barr JR, Maggio VL, Barr DB, Turner WE, Sjodin A, Sandau CD, et al. 2003. New high-resolution mass spectrometric approach for the measurement of polychlorinated biphenyls and organochlorine pesticides in human serum. *J Chromatogr B Analyt Technol Biomed Life Sci* 794:137-148.
- Bat-Erdene U, Metcalfe A, McDonald SW, Tough SC. 2013. Validation of Canadian mothers' recall of events in labour and delivery with electronic health records. *BMC Pregnancy Childbirth* 13 Suppl 1:S3.
- Bernert JT, Turner WE, Patterson DG, Jr., Needham LL. 2007. Calculation of serum "total lipid" concentrations for the adjustment of persistent organohalogen toxicant measurements in human samples. *Chemosphere* 68:824-831.
- Bernert JT, Jr., Turner WE, Pirkle JL, Sosnoff CS, Akins JR, Waldrep MK, et al. 1997. Development and validation of sensitive method for determination of serum cotinine in smokers and nonsmokers by liquid chromatography/atmospheric pressure ionization tandem mass spectrometry. *Clin Chem* 43:2281-2291.
- Bloom MS, Buck Louis GM, Schisterman EF, Liu A, Kostyniak PJ. 2007. Maternal serum polychlorinated biphenyl concentrations across critical windows of human development. *Environ Health Perspect* 115:1320-1324.
- Buck Louis GM, Schisterman EF, Sweeney AM, Wilcosky TC, Gore-Langton RE, Lynch CD, et al. 2011. Designing prospective cohort studies for assessing reproductive and developmental toxicity during sensitive windows of human reproduction and development--the LIFE Study. *Paediatr Perinat Epidemiol* 25:413-424.

- Buck Louis GM, Sundaram R, Schisterman EF, Sweeney AM, Lynch CD, Gore-Langton RE, et al. 2013. Persistent environmental pollutants and couple fecundity: the LIFE study. *Environ Health Perspect* 121:231-236.
- Buka SL, Goldstein JM, Sparto E, Tsuang MT. 2004. The retrospective measurement of prenatal and perinatal events: accuracy of maternal recall. *Schizophr Res* 71:417-426.
- Centers for Disease Control and Prevention. 2013. Fourth National Report on Human Exposure to Environmental Chemicals. Updated Tables, Tables, September 2013. National Center for Environmental Health; Division of Laboratory Sciences, Atlanta, GA.
- Chapin RE, Robbins WA, Schieve LA, Sweeney AM, Tabacova SA, Tomashek KM. 2004. Off to a good start: the influence of pre- and periconceptional exposures, parental fertility, and nutrition on children's health. *Environ Health Perspect* 112:69-78.
- Cliver SP, Goldenberg RL, Cutter GR, Hoffman HJ, Davis RO, Nelson KG. 1995. The effect of cigarette smoking on neonatal anthropometric measurements. *Obstet Gynecol* 85:625-630.
- Cogswell ME, Yip R. 1995. The influence of fetal and maternal factors on the distribution of birthweight. *Semin Perinatol* 19:222-240.
- Cook PS, Sato T, Buchanan D.L. 2001. Disruption of Steroid Hormone Signaling by PCBs. In: *PCBs: Recent Advances in Environmental Toxicology and Health Effects* (Robertson L.W., Hansen L.G., eds.). The University of Kentucky.
- Cordier S. 2008. Evidence for a role of paternal exposures in developmental toxicity. *Basic Clin Pharmacol Toxicol* 102:176-181.
- Curley JP, Mashoodh R, Champagne FA. 2011. Epigenetics and the origins of paternal effects. *Horm Behav* 59:306-314.
- Eskenazi B, Harley K, Bradman A, Weltzien E, Jewell NP, Barr DB, et al. 2004. Association of in utero organophosphate pesticide exposure and fetal growth and length of gestation in an agricultural population. *Environ Health Perspect* 112:1116-1124.
- Farhang L, Weintraub JM, Petreas M, Eskenazi B, Bhatia R. 2005. Association of DDT and DDE with birth weight and length of gestation in the Child Health and Development Studies, 1959-1967. *Am J Epidemiol* 162:717-725.
- Foster WG, Gregorovich S, Morrison KM, Atkinson SA, Kubwabo C, Stewart B, et al. 2011. Human maternal and umbilical cord blood concentrations of polybrominated diphenyl ethers. *Chemosphere* 84:1301-1309.

- Fullston T, Ohlsson Teague EM, Palmer NO, DeBlasio MJ, Mitchell M, Corbett M, et al. 2013. Paternal obesity initiates metabolic disturbances in two generations of mice with incomplete penetrance to the F2 generation and alters the transcriptional profile of testis and sperm microRNA content. *FASEB J* 27:4226-4243.
- Givens ML, Small CM, Terrell ML, Cameron LL, Michels BH, Tolbert PE, et al. 2007. Maternal exposure to polybrominated and polychlorinated biphenyls: infant birth weight and gestational age. *Chemosphere* 69:1295-1304.
- Govarts E, Nieuwenhuijsen M, Schoeters G, Ballester F, Bloemen K, de BM, Chevrier C, et al. 2012. Birth weight and prenatal exposure to polychlorinated biphenyls (PCBs) and dichlorodiphenyldichloroethylene (DDE): a meta-analysis within 12 European Birth Cohorts. *Environ Health Perspect* 120:162-170.
- Harley KG, Chevrier J, Schall RA, Sjodin A, Bradman A, Eskenazi B. 2011. Association of prenatal exposure to polybrominated diphenyl ethers and infant birth weight. *Am J Epidemiol* 174:885-892.
- Karmaus W, Zhu X. 2004. Maternal concentration of polychlorinated biphenyls and dichlorodiphenyl dichloroethylene and birth weight in Michigan fish eaters: a cohort study. *Environ Health* 3:1.
- Kezios KL, Liu X, Cirillio PM, Kalantzi OI, Wang Y, Petreas MX, et al. 2012. Prenatal polychlorinated biphenyl exposure is associated with decreased gestational length but not birth weight: archived samples from the Child Health and Development Studies pregnancy cohort. *Environ Health* 11:49.
- Kuklenyik Z, Needham LL, Calafat AM. 2005. Measurement of 18 perfluorinated organic acids and amides in human serum using on-line solid-phase extraction. *Anal Chem* 77:6085-6091.
- Lawson CC, Schnorr TM, Whelan EA, Deddens JA, Dankovic DA, Piacitelli LA, et al. 2004. Paternal occupational exposure to 2,3,7,8-tetrachlorodibenzo-p-dioxin and birth outcomes of offspring: birth weight, preterm delivery, and birth defects. *Environ Health Perspect* 112:1403-1408.
- Leonardi-Bee J, Britton J, Venn A. 2011. Secondhand smoke and adverse fetal outcomes in nonsmoking pregnant women: a meta-analysis. *Pediatrics* 127:734-741.

- Llop S, Ballester F, Vizcaino E, Murcia M, Lopez-Espinosa MJ, Rebagliato M, et al. 2010. Concentrations and determinants of organochlorine levels among pregnant women in Eastern Spain. *Sci Total Environ* 408:5758-5767.
- Lohman TG, Roche AF, Martorell R, eds. 1988. *Anthropometric Standardization Reference Manual*. Champaign, IL:Human Kinetics Books.
- Longnecker MP, Klebanoff MA, Brock JW, Guo X. 2005. Maternal levels of polychlorinated biphenyls in relation to preterm and small-for-gestational-age birth. *Epidemiology* 16:641-647.
- Mattison DR. 2010. Environmental exposures and development. *Curr Opin Pediatr* 22:208-218.
- Mayer C, Joseph KS. 2013. Fetal growth: a review of terms, concepts and issues relevant to obstetrics. *Ultrasound Obstet Gynecol* 41:136-145.
- Mazdai A, Dodder NG, Abernathy MP, Hites RA, Bigsby RM. 2003. Polybrominated diphenyl ethers in maternal and fetal blood samples. *Environ Health Perspect* 111:1249-1252.
- Michalek JE, Rahe AJ, Boyle CA. 1998. Paternal dioxin, preterm birth, intrauterine growth retardation, and infant death. *Epidemiology* 9:161-167.
- Mikes O, Cupr P, Kohut L, Krskova A, Cerna M. 2012. Fifteen years of monitoring of POPs in the breast milk, Czech Republic, 1994-2009: trends and factors. *Environ Sci Pollut Res Int* 19:1936-1943.
- Murphy LE, Gollenberg AL, Buck Louis GM, Kostyniak PJ, Sundaram R. 2010. Maternal serum preconception polychlorinated biphenyl concentrations and infant birth weight. *Environ Health Perspect* 118:297-302.
- Olsen GW, Butenhoff JL, Zobel LR. 2009. Perfluoroalkyl chemicals and human fetal development: an epidemiologic review with clinical and toxicological perspectives. *Reprod Toxicol* 27:212-230.
- Olshan AF, Faustman EM. 1993. Male-mediated developmental toxicity. *Annu Rev Public Health* 14:159-181.
- Pan IJ, Daniels JL, Goldman BD, Herring AH, Siega-Riz AM, Rogan WJ. 2009. Lactational exposure to polychlorinated biphenyls, dichlorodiphenyltrichloroethane, and dichlorodiphenyldichloroethylene and infant neurodevelopment: an analysis of the pregnancy, infection, and nutrition babies study. *Environ Health Perspect* 117:488-494.

- Phillips DL, Pirkle JL, Burse VW, Bernert JT, Jr., Henderson LO, Needham LL. 1989. Chlorinated hydrocarbon levels in human serum: effects of fasting and feeding. *Arch Environ Contam Toxicol* 18:495-500.
- Pope DP, Mishra V, Thompson L, Siddiqui AR, Rehfuess EA, Weber M, Bruce NG. 2010. Risk of low birth weight and stillbirth associated with indoor air pollution from solid fuel use in developing countries. *Epidemiol Rev* 32:70-81.
- Rodriguez-Dozal S, Riojas RH, Hernandez-Avila M, Van OJ, Weber JP, Needham LL, Trip L. 2012. Persistent organic pollutant concentrations in first birth mothers across Mexico. *J Expo Sci Environ Epidemiol* 22:60-69.
- Rubin DB. 1996. Multiple Imputation After 18+ Years. *J Amer Statist Assoc* 91:473-489.
- Rudge CV, Sandanger T, Rollin HB, Calderon IM, Volpato G, Silva JL, et al. 2012. Levels of selected persistent organic pollutants in blood from delivering women in seven selected areas of Sao Paulo State, Brazil. *Environ Int* 40:162-169.
- Sandau CD, Sjodin A, Davis MD, Barr JR, Maggio VL, Waterman AL, et al. 2003. Comprehensive solid-phase extraction method for persistent organic pollutants. Validation and application to the analysis of persistent chlorinated pesticides. *Anal Chem* 75:71-77.
- Schisterman EF, Vexler A, Whitcomb BW, Liu A. 2006. The limitations due to exposure detection limits for regression models. *Am J Epidemiol* 163:374-383.
- Shah PS. 2010. Paternal factors and low birthweight, preterm, and small for gestational age births: a systematic review. *Am J Obstet Gynecol* 202:103-123.
- Shinwell ES, Shlomo M. 2003. Measured length of normal term infants changes over the first two days of life. *J Pediatr Endocrinol Metab* 16:537-540.
- Sparks JW, Ross JC, Cetin I. 1998. Fetal and neonatal physiology. Philadelphia, USA:W.B. Saunders.
- Sweeney AM, Symanski E. 2007. The influence of age at exposure to PBBs on birth outcomes. *Environ Res* 105:370-379.
- Tan J, Loganath A, Chong YS, Obbard JP. 2009. Exposure to persistent organic pollutants in utero and related maternal characteristics on birth outcomes: a multivariate data analysis approach. *Chemosphere* 74:428-433.
- Tanabe S, Kunisue T. 2007. Persistent organic pollutants in human breast milk from Asian countries. *Environ Pollut* 146:400-413.

- Wang RY, Jain RB, Wolkin AF, Rubin CH, Needham LL. 2009. Serum concentrations of selected persistent organic pollutants in a sample of pregnant females and changes in their concentrations during gestation. *Environ Health Perspect* 117:1244-1249.
- Washino N, Saijo Y, Sasaki S, Kato S, Ban S, Konishi K, et al. 2009. Correlations between prenatal exposure to perfluorinated chemicals and reduced fetal growth. *Environ Health Perspect* 117:660-667.
- Windham G, Fenster L. 2008. Environmental contaminants and pregnancy outcomes. *Fertil Steril* 89:e111-e116.
- Wolff MS, Engel S, Berkowitz G, Teitelbaum S, Siskind J, Barr DB, et al. 2007. Prenatal pesticide and PCB exposures and birth outcomes. *Pediatr Res* 61:243-250.
- Wu K, Xu X, Liu J, Guo Y, Li Y, Huo X. 2010. Polybrominated diphenyl ethers in umbilical cord blood and relevant factors in neonates from Guiyu, China. *Environ Sci Technol* 44:813-819.

Table 1. Persistent organic pollutants measured in study population, LIFE Study, 2005-2008.

Persistent organic pollutants	Compounds or congeners
Polybrominated biphenyl (PBB)	153
Organochlorine pesticides	Hexachlorobenzene (HCB), β-hexachlorocyclohexane (β-HCH), γ-hexachlorocyclohexane (γ-HCH), oxychlorodane, <i>trans</i> -nonachlor, mirex, <i>o,p'</i> -DDT, <i>p,p'</i> -DDT, and <i>p,p'</i> -DDE
Polybrominated diphenyl ethers (PBDEs)	17, 28, 47, 66, 85, 99, 100, 153, 154, 183
Polychlorinated biphenyls (PCB)	28, 44, 49, 52, 66, 74, 87, 99, 101, 105, 110, 114, 118, 128, 138, 146, 149, 151, 153, 156, 157, 167, 170, 172, 177, 178, 180, 183, 187, 189, 194, 195, 196, 201, 206, 209
Perfluoroalkyl chemicals (PFCs)	2-(n-ethyl-perfluorooctane sulfonamide) acetate (Et-PFOSA-AcOH), 2-(N-methyl- perfluorooctane sulfonamide) acetate (Me- PFOSA-AcOH), perfluorodecanoate (PFDeA), perfluorononanoate (PFNA), perfluorooctane sulfonamide (PFOSA), perfluorooctane sulfonate (PFOS) and perfluorooctanoate (PFOA)

Table 2. Description^a of study cohort by partner among those with a singleton delivery (n = 234), LIFE Study, 2005-2009.

Characteristic	Mothers n (%) or mean ± SD	Fathers n (%) or mean ± SD
Race/ethnicity		
Non-Hispanic white	194 (84)	198 (85)
Non-Hispanic black	2 (1)	4 (2)
Hispanic	20 (9)	20 (9)
Other	16 (7)	12 (5)
Education		
< High school	0 (0)	2 (1)
High school/equivalent	9 (4)	5 (2)
College	223 (96)	225 (97)
Health insurance		
No	5 (2)	10 (4)
Yes	227 (98)	223 (96)
Smoking status at baseline*		
Active (cotinine ≥ 100 ng/ml)	11 (5)	24 (10)
Passive (cotinine < 100 ng/ml)	219 (95)	205 (90)
Cigarettes smoked (9-12 wks)		
None	227 (98.8)	--
Less than 10	2 (0.8)	--
More than 10	1 (0.4)	--
Alcohol use at baseline^{b, *}		
No	52 (22)	31 (13)
Yes	182 (78)	203 (87)
Alcohol use (9-12 wks)		
None	229 (99.6)	--
1 drink/week	1 (0.4)	--
Age (years)*	29.8 ± 3.7	31.5 ± 4.6
Body mass index (kg/m²)*	26.4 ± 6.5	29.3 ± 5.3
Gravidity	1.1 ± 1.2	1.0 ± 1.1
Parity	0.7 ± 0.8	0.69 ± 0.8

^aAll characteristics are self-reported except for body mass index. Missing covariate data was not included in table. ^bAt baseline participants reported whether they had consumed alcohol in the last 12 months.

*Chi-Square test p-value <0.05.

Table 3. Adjusted^a mean changes (β) and their 95% confidence intervals for each birth size measure per 1-SD increase in ln-transformed chemical concentration^b by partner and infant gender, LIFE Study, 2005-2009.

Outcome	Maternal, girl β (95% CI)	Maternal, boy β (95% CI)	Paternal, girl β (95% CI)	Paternal, boy β (95% CI)
Birth weight (grams) ^c				
<i>o,p'</i> -DDT	-195.39 (-351.25, -39.52)*	-6.11 (-93.02, 80.80)*	-49.28 (-153.83, 55.27)	4.32 (-86.15, 94.79)
PBDE-28	-151.33 (-298.56, -4.10)	-64.65 (-164.92, 35.63)	-30.85 (-154.83, 93.14)	14.99 (-99.94, 129.93)
PBDE-66	-21.98 (-141.29, 97.33)*	125.04 (18.16, 231.92)*	-39.80 (-152.57, 72.96)	-47.85 (-173.89, 78.19)
PBDE-99	52.08 (-120.80, 224.96)	133.39 (9.12, 257.37)	17.53 (-123.74, 158.80)	59.43 (-90.47, 209.33)
PBDE-183	-84.60 (-154.39, -14.82)*	85.21 (-32.32, 202.74)*	-92.13 (-173.44, -10.82)	21.32 (-85.27, 127.91)
PCB-138	-82.30 (-219.22, 54.61)	-149.6 (-285.16, -14.06)	-69.04 (-191.78, 53.71)	-103.02 (-264.04, 57.99)
PCB-153	-90.94 (-240.89, 59.01)	-169.93 (-317.32, -22.53)	-29.33 (-164.37, 105.70)	-68.77 (-226.45, 88.91)
PCB-167	-61.69 (-172.52, 49.15)	-129.24 (-228.16, -30.31)	-97.49 (-187.45, -7.54)	-38.24 (-139.86, 63.37)
PCB-170	-80.87 (-223.93, 62.18)	-153.69 (-288.45, -18.92)	-16.85 (-144.38, 110.67)	-119.29 (-268.37, 29.79)
PCB-172	68.59 (-48.81, 185.99)	-37.21 (-148.16, 73.74)	-35.87 (-143.12, 71.38)	-166.89 (-311.19, -22.60)
PCB-195	-18.46 (-128.10, 91.18)	-137.73 (-259.57, -15.89)	-6.94 (-102.96, 89.07)*	-148.39 (281.69, -15.08)*
PCB-209	-24.96 (-135.66, 85.74)	-98.88 (-187.14, -10.61)	-24.49 (-124.53, 75.56)	-0.80 (-115.85, 114.24)
PFOSA	-8.80 (-93.55, 75.95)	-104.23 (-194.16, -14.30)	10.48 (-85.29, 106.26)	-73.76 (-154.43, 6.91)
Length (cm) ^d				
γ -HCH	-0.59 (-1.14, -0.03)*	0.34 (-0.17, 0.84)*	-0.51 (0.98, -0.04)*	0.33 (-0.20, 0.86)*
PBDE-28	-1.14 (-2.00, -0.28)*	-0.18 (-0.76, 0.41)*	-0.28 (-1.02, 0.46)	0.00 (-0.67, 0.67)
PBDE-99	0.25 (-0.76, 1.27)	0.76 (0.04, 1.48)	0.18 (-0.65, 1.01)	0.44 (-0.43, 1.31)
PCB-167	-0.47 (-1.12, 0.19)	-0.42 (-1.00, 0.16)	-0.57 (-1.12, -0.02)	-0.11 (-0.70, 0.49)
Head circumference (cm) ^e				
HCB	0.10 (-0.40, 0.61)	0.44 (0.01, 0.87)	0.12 (-0.40, 0.63)	-0.22 (-0.63, 0.19)
β -HCH	-1.47 (-2.33, -0.61)*	-0.22 (-0.58, 0.14)*	0.23 (-0.68, 1.13)	-0.16 (-0.78, 0.46)
<i>o,p'</i> -DDT	-0.78 (-1.48, -0.09)	-0.06 (-0.47, 0.35)	-0.14 (-0.59, 0.32)	0.20 (-0.28, 0.67)
PBDE-28	-1.05 (-1.73, -0.38)*	-0.24 (-0.67, 0.19)*	0.02 (-0.57, 0.61)	0.18 (-0.33, 0.69)
PBDE-66	-0.17 (-0.76, 0.41)*	0.60 (0.02, 1.18)*	0.10 (-0.39, 0.59)	0.33 (-0.26, 0.92)
PBDE-85	0.34 (-0.78, 1.45)*	1.04 (0.04, 2.03)*	-0.01 (-0.83, 0.80)	0.16 (-0.76, 1.09)

Outcome	Maternal, girl β (95% CI)	Maternal, boy β (95% CI)	Paternal, girl β (95% CI)	Paternal, boy β (95% CI)
PBDE-99	0.27 (-0.48, 1.02)	0.91 (0.23, 1.60)	0.10 (-0.52, 0.71)	0.31 (-0.38, 0.99)
PCB-128	0.08 (-0.30, 0.45)*	-0.86 (-1.45, -0.10)*	-0.18 (-0.61, 0.25)	-0.66 (-1.31, -0.01)
PCB-138	-0.65 (-1.25, -0.05)	-0.67 (-1.67, -0.06)	-0.32 (-0.86, 0.22)	-0.56 (-1.30, 0.17)
PCB-153	-0.65 (-1.30, 0.01)	-0.78 (-1.27, -0.08)	0.06 (-0.59, 0.71)	-0.22 (-0.79, 0.36)
PCB-157	-0.22 (-0.62, 0.18)	-0.17 (-0.66, 0.32)	-0.06 (-0.46, 0.34)	-0.54 (-1.01, -0.06)
PCB-167	-0.04 (-0.55, 0.46)	-0.47 (-0.95, 0.00)	-0.45 (-0.86, -0.03)	-0.32 (-0.80, 0.16)
PCB-201	0.51 (0.08, 0.93)	0.28 (-0.31, 0.87)	0.19 (-0.22, 0.61)	-0.32 (-1.08, 0.44)
PCB-206	0.52 (0.06, 0.98)	0.16 (-0.30, 0.63)	0.16 (-0.34, 0.66)	-0.38 (-1.17, 0.41)
Ponderal Index (g/cm ³) ^d				
γ -HCH	0.09 (0.03, 0.16)*	-0.01 (-0.07, 0.05)*	0.08 (0.02, 0.13)	0.00 (-0.07, 0.06)
<i>p,p'</i> -DDE	0.03 (-0.07, 0.13)	0.03 (-0.04, 0.09)	0.12 (0.02, 0.22)*	0.01 (-0.06, 0.07)*
PCB-138	-0.10 (-0.20, -0.01)	-0.13 (-0.23, -0.04)	-0.09 (-0.18, 0.00)	-0.13 (-0.24, -0.02)
PCB-156	-0.04 (-0.11, 0.03)	-0.05 (-0.13, 0.03)	-0.08 (-0.16, -0.01)	-0.11 (-0.20, -0.03)
PCB-157	-0.03 (-0.09, 0.04)	-0.04 (-0.12, 0.03)	-0.03 (-0.09, 0.04)	-0.08 (-0.16, -0.01)
PCB-170	-0.10 (-0.20, 0.00)	-0.10 (-0.20, -0.01)	-0.02 (-0.11, 0.07)	-0.03 (-0.14, 0.07)
PCB-172	-0.05 (-0.13, 0.03)	-0.09 (-0.17, -0.02)	-0.01 (-0.09, 0.07)	-0.03 (-0.13, 0.07)
Et-PFOA-AcOH	-0.09 (-0.16, -0.02)	-0.02 (-0.08, 0.04)	-0.04 (-0.10, 0.03)	-0.07 (-0.16, 0.03)

^aResults are only presented for chemicals for which at least one statistically significant association between pollutants and birth size measures were estimated. Models are adjusted for maternal and paternal serum lipids, serum cotinine, maternal pre-pregnancy BMI (kg/m²), maternal age, difference in parental age, infant gender, the individual and partner sum of remaining chemical concentrations in each chemical's respective class. ^bRestricted to chemicals with a significant association with fetal growth outcomes. ^cData for 113 boys and 117 girls were available for analysis. ^dData for 113 boys and 116 girls were available for analysis. ^eData for 90 boys and 91 girls were available for analysis. * $p < 0.05$ for parent concentration and infant gender interaction term.